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CLINICAL-MICROBIOLOGIC MONITORING OF ETIOLOGIC STRUCTURE OF PYELONEPHRITIS IN CHILDREN OF DNIPROPETROVSK REGION

In the structure of urinary tract infections pyelonephritis presents the most prevalent clinical problem of pediatric nephrology. Gradual increase of resistance to antimicrobial drugs in children with pyelonephritis (PN) causes great concern [7, 812; 8, 225; 9, 179]. So, knowledge of PN etiology and tactic approach to the choice of etiotropic therapy in children is important in the practice of pediatrician and general practitioner [3,213, 10, 546]. According to WHO recommendations to improve usage of antibacterial means a permanent supervision over clinical practice, revealing causative agents, favoring inadequate administration of antibiotics and rendering care in treatment-diagnostic strategy is necessary. These are the tasks of independent pharmacologic-epidemiologic investigations, which make it possible to obtain objective data and to develop effective interventions for the adequate usage of antibiotics [10, 547]. Antibiotic must be chosen considering the following main criteria: spectrum of its antimicrobial activity in vitro, regional level of causative agents, resistance to antibiotic, proved efficiency in the controlled clinical study. [2, 3; 12, 315].

The aim of our work was defining modern structure, sensitivity and resistance of urologic pathogens in children with PN depending on age, based on performing clinical-microbiologic monitoring for widening possibilities of effective rational antibacterial therapy.

Materials and methods.

Duration of monitoring of structure, sensitivity and resistance of urologic pathogens in children and adolescents with PN, residents of Dnipropetrovsk region, made up 10 years. There has been performed analysis of 569 PN cases of children and adolescents, in-patients of nephrology unit of Dnipropetrovsk regional clinical pediatric hospital of Dnipropetrovsk city, of them 387 cases - in 2001-2009 years and 182 – in 2010-2012 years [1, 193].

160 PN patients who have been under supervision in 2010-2012 years were divided into age-related groups: at the age of 1-6 years – 29 children (9 boys and 20 girls), at the age of 7-10 years - 27 children (2 boys, 25 girls); at the age of 11-17 years - 104 children (46 boys, 46 girls). Group of comparison included 22 children with acute PN.

All in-patient children underwent clinical, laboratory and instrumental examination in accordance with «Regimen protocol on pediatric urinary

infections and tubular-interstitial nephritis and urinary system infections» (Order of HM of Ukraine № 627 from 03.11.2008) and Guidelines on Paediatric Urology [5, 6; 11, 25].

Laboratory investigation included total blood count in dynamics of the disease course, biochemical findings of inflammatory process activity (total protein and protein fractions, C-reactive protein), urea and creatinin content in serum, investigation of urinary sediment (common urine analysis, urine analysis by Nechiporenko).

In the work most of the focus is revealing specific features of up-to-date spectrum of urologic pathogens, their sensitivity and antibiotic resistance in chronic PN children considering age to provide rational antibacterial therapy in the following.

Urine culture for flora with quantitative assessment of bacteriuria stage and antibiogram was carried out in all patients. Urine culture was carried out before antibacterial therapy. Defining sensitivity and antibiotic resistance was carried out in bacteriologic laboratory by disk diffusion test on AGV medium [6, 156].

Mathematic and statistical processing of the data obtained was performed on PC by means of statistic program package Microsoft Excel 7.0. Digital results were processed statistically by means of alternative and variation analysis methods. Probability of variable standards was assessed by parametric Fisher-Student's criterion [4, 24].

Results and discussion.

Spectrum of rate of microbe causative agents cultured in urine in acute PN in children under supervision over the period from 2010 to 2012 was characterized by a somewhat predominance of E. coli (26,3%) and enterococci (15,8%). Somewhat rarely (by 10,5%) other gram-negative causative agents were cultured: Citrobacter, Ps.aeroginosa, as well as gram-positive Streptococcus and Candida fungi.

Performed analysis of age-related peculiarities of etiologic structure of chronic PN showed that in children aged from 1 to 6 years in PN exacerbation, reliably more often ($p<0,05$) than in children with acute PN E. coli was cultured - 58,3% of cases. Less frequently causative agents of enterobacteria (Enterococcus spp.) – 25,0% and Klebsiella pn. - 8,3% were cultured. Citrobacter and Streptococcus (4,2%) were cultured rarely in pre-school children with chronic PN.

In chronic PN in junior schoolchildren (aged from 7 to 10 years) rate of cultured urinary pathogens had some differences from the group of pre-school children. Reliably more often than in pre-school children, staphylococci (Staphylococcus hem. and Staphylococcus epid.) 17,4% ($p<0,05$) were cultured under such an obvious predominance of E. coli - 60,9% in the microbe spectrum and the same incidence of cultured Klebsiella pn. (8,8%).

In chronic PN in senior schoolchildren (aged from 11 to 17 years) the rate of cultured microbe pathogens in urine had some differences from the group of junior schoolchildren. In preserved predominance of E. Coli in microbe spectrum this causative agent was cultured reliably rarely – 36,2% of cases ($p<0,05$) in senior schoolchildren. Staphylococci (Staphylococcus hem.and Staphylococcus epid.) – 17,4%, ranked second at this age, but just as in pre-school children amount of cultured causative agents of enterobacteria (Enterococcus spp.) – 17,0% and Klebsiella pn. -14,9% was increasing.

Integrally, in children with chronic PN regardless of age, in the spectrum of urinary pathogens E. Coli (47,9%) prevailed. Reliably more rarely ($p<0,01$) Grp+ pathogens - Enterococcus spp. (14,9%), staphylococci (Staphylococcus hem. and Staphylococcus epid.) - 12,8% and Gr- Klebsiella pn. - 11,6% of cases were cultured.

Carrying out monitoring and comparing obtained results with the data of examined children of Dnipropetrovsk region in 2001-2009, the following dynamics was defined. In the structure of pathogens of infection in exacerbation of chronic PN just as three years before Gr- flora, presented by enteric bacterium, prevailed (47,9% and 47,2% of cases correspondingly). Somewhat more rarely in children with chronic PN Gr+ cocci (staphylococci, streptococci, enterococci) – 29,8% of cases occurred. Grp+ cocci were cultured in urine more often - in 40,7% of cases ($p>0,05$) three years before. More rarely in chronic PN such pathogens of enterobacteria as Klebsiella, Citrobacter, Proteus, Enterobacterium were cultured, totally in 22,3% of cases. This finding was less, being 12,1% of cases three years before, $p>0,05$.

Results of microbiologic monitoring showed that over the last 10 years in the structure of urologic pathogens, cultured in chronic PN in children of Dnipropetrovsk region, a number of isolated Gr- microflora, pathogens of entorobacterium increased, up to 70,2%, herewith proportion of E. coli in the etiologic structure dominates with the previous incidence. Incidence of other isolated pathogens of enterobacteria grew 2 times, herewith incidence of isolated Klebsiella pn. (from 1,7% to 11,6%) grew 7 times. Number of isolated Gr+ microflora (staphylococci, streptococci, enterococci) decreased from 40,7% to 29,8% of cases, $p<0,05$.

Carried out comparative analysis of sensitivity of main PN pathogens to antibiotics in children by the data of bacteriologic studies showed, that the highest incidence of sensitivity of the main PN pathogen, E.coli, was to amikacin (59%, in 2001-2009 years - 71,6%, $p>0,05$), levomycetin (57%, in 2001-2009 - 73,0%, $p>0,05$) and cefuroxime (41%, in 2009 – 39,6%, $p>0,1$). Herewith, as compared with the data of 2001-2009 years, sensitivity incidence to ceftriaxone significantly decreased– from 92,4% to 24% ($p<0,001$), and to furaginum – from 78,4% to 35% ($p<0,01$); this raises doubts about advisability of using the latest antimicrobial means for starting empiric therapy in treatment of PN children at present-day. Sensitivity incidence of E. coli to ampicillin was

low just as 10 years before (38%, in 2009 – 31,4%, p>0,05). Comparative analysis of E.coli resistance to antibiotics showed that in chronic PN this pathogen was mostly resistant to ampicillin and furaginum (16%), herewith resistance incidence to ampicillin decreased by 3 times as compared with 2001-2009 years. Only in single cases there was registered E.coli resistance to meropenem (3%), imipenem (6%).

Currently, Pr. mirabilis was resistant to amikacin and ciprofloxacin in 100% of cases, to cefuroxime and levomycetin - in 50% of cases. Herewith Pr. mirabilis was resistant to ampicillin and levomycetin in 100% of cases, to cefuroxime and furaginum – in 50% of cases. It should be noted that resistance incidence to levomycetin grew by 3 times as compared with the data of the year 2009.

In 100% of cases Ps. aeroginosa was sensitive to amikacin, more rarely (50%) – to cefuroxime, imipenem and levofloxacin. Low sensitivity incidence of this microorganism was to ceftriaxone, meropenem and ceftriaxone - by 25% of cases. As for resistance, it should be mentioned that currently Ps. aeroginosa in 50% of cases was resistant to cefuroxime and furagin and in 25% of cases –to ceftriaxone.

Conclusion.

Carried out monitoring studies of changes of urologic pathogens sensitivity and resistance made it possible to draw a conclusion that in administering empiric initial treatment of acute PN or in exacerbations of chronic PN in children, with the greatest probability of E.coli and Enterobacteria to be the causative agents, preferences should be given to cephalosporins of the II generation – cefuroxime and those of the III one – cefpodoxime and cefixime. In severe cases combination of these cephalosporins with amikacin or levofloxacin may be effective (in children over 12 years of age). Currently, both gram- enterobacateria and gram+ staphylococci, streptococci, enterococci are equally sensitive to latter antibiotics.

Regularly, every 3-5 years it is necessary to carry out regional microbiologic monitoring of sensitivity and resistance of urologic pathogenic microflora in PN children.

Literature

1. Vakulenko L.I., Kondratiev V. O., Riznyk T.K. Vikova etiologichna struktura pielonefritu u ditey i racionalna antebakterialna terapiya. Sovremennaya pediatriya.-2010.-№4(32).-p.193-196.
2. Performance Standards for Antimicrobial Susceptibility Testing; Twenty-Second Informational Supplement M100-S22 Vol. 32 No. 3 Replaces M100-S21 Vol. 31 No. 1 - 188 p.

3. Ivanov D.D., O.M. Korzh. Nefrologiya v praktyci simeynogo likarya: navchalno-metodychnyi posibnyk- 3-tye vyd., pererobl. i dopovn. Donetsk: Vydavets Zaslavвsky O.Yu., 2014. — 464 p.
4. Platonov A.E. Statistichesky analiz v medicine I biologii /A.E.Platonov. – M.: RAMN, 2000. – 51p.
5. Regimen protocol on pediatric urinary infections and tubular-interstitial nephritis and urinary system infections. Order of HM of Ukraine № 627 from 03.11.2008) [E-dokument]: http : //-www.moz.gov.ua. — 25 p.
6. Stecyuk O.U., Reshedko G.K. Sravnenie rezultatov opredeleniya chuvstvitelnosti k antibiotikam gramotricatelnyh aerobnyh bakteriy disko-diffuzionnym metodom na sryedye AGV n agarye Mullera-Hinton. Klinicheskaya mikrobiologiya I antimikrobnaya himioterapiya.-2004.-т. 6.-№2.-p.155-67.
7. Amira PA, Dusan P, Brankica SD, Svetlana B. Trend of antibiotic resistance in children with first acute pyelonephritis. Indian Pediatr. 2011 Oct;48(10):812-3.
8. de Lucas Collantes C. Cela Alvargonzalez J., Angulo Chacón A.M. et all. Urinary tract infections: antibiotic resistance and clinical follow up. An Pediatr (Barc). 2012 Apr;76(4):224-8.
9. Peco-Antić A., Paripović D, Buljugić S. et all. Antibiotic resistance of uropathogens in newborns and young children with acute pyelonephritis. Srp Arh Celok Lek. 2012 Mar-Apr;140(3-4):179-183.
10. Stein R, Dogan HS, Hoebeke P, Kočvara R, Nijman RJ, Radmayr C, Tekgül S. Urinary Tract Infections in Children: EAU/ESPU Guidelines. //Eur Urol. 2015 Mar;67(3):546-58.
11. Tekgül S., Dogan H.S., Erdem E. et all. Guidelines on Paediatric Urology. 2015: 22-30.
12. Joan L Robinson, Jane C Finlay, Mia Eileen Lang, Robert Bortolussi. Urinary tract infections in infants and children: Diagnosis and management Paediatr Child Health. 2014 Jun-Jul; 19(6): 315–319.